18; and page 22, line 1 to page 23, line 9; claim 51: page 33, lines 12-14. Accordingly, no new matter is added.

Applicants respectfully request entry of the amendment to the specification and the above new claims.

## III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCSF048CON.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: May 22, 2001

By: _____
Paula A. Borden
Registration No. 42,344

BOZICEVIC, FIELD & FRANCIS LLP
200 Middlefield Road, Suite 200
Menlo Park, CA 94025
Telephone: (650) 327-3400
Facsimile: (650) 327-3231

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# VERSION WITH MARKINGS TO SHOW CHANGES MADE

## IN THE SPECIFICATION

On page 1, please enter the following amendment to the paragraph beginning on line 3:

CROSS-REFERENCE

This application is a continuation of U.S. Application serial no. 09/254,988, filed March 16, 1999, which was a national stage filing under 35 U.S.C.§371 of PCT Application No. PCT/US97/16523, filed September 18, 1997, which International Application was published by the International Bureau in English on March 26, 1998; and which is a continuation-in-part of U.S. Application serial no. 08/717,084, filed September 19, 1996, now U.S. Patent No. 6,225,290; which [application is] applications are hereby incorporated by reference herein and to which applications priority is claimed.

## IN THE CLAIMS

Please cancel claims 1-17 without prejudice to renewal.
Please enter new claims 18-51, as shown below.

--18. (New) A method of delivering a secreted protein into the bloodstream of a mammalian subject, the method comprising:

introducing into the gastrointestinal tract of a mammalian subject by oral administration a construct comprising:

c) a nucleic acid molecule comprising a coding sequence encoding a protein; and

d) a promoter sequence operably linked to the coding sequence, wherein said construct is not packaged in a viral particle, said introducing resulting in introduction of the construct into an intestinal epithelial cell, production of the encoded protein in the intestinal epithelial cell and secretion of the protein from the cell and into the bloodstream of the subject.

19. (New) The method of claim 18, wherein the protein is a fusion protein.

20. (New) The method of claim 18, wherein the protein is altered relative to a wild-type protein.

21. (New) The method of claim 18, wherein the nucleic acid molecule is formulated as a liquid, a solid, a pill, a capsule, a tablet, a solution, a gel, a syrup, a slurry or a suspension.

22. (New) The method of claim 18, wherein the nucleic acid molecule is formulated to facilitate swallowing.

23. (New) The method of claim 18, wherein the nucleic acid molecule is formulated with an agent that protects against degradation.

24. (New) The method of claim 18, wherein the nucleic acid molecule is formulated as a time-release formulation.

25. (New) The method of claim 18, wherein the nucleic acid molecule is associated with an agent that facilitates delivery to the target cell.

26. (New) The method of claim 18, wherein the protein is an immunotherapeutic protein.

27. (New) The method of claim 18, wherein the protein increases an immune response.

28. (New) The method of claim 18, wherein the protein induces immune tolerance.

29. (New) The method of claim 18, wherein the protein is an antigen.

30. (New) The method of claim 29, wherein the antigen is a viral antigen.

31. (New) The method of claim 29, wherein the antigen is a bacterial antigen.

32. (New) The method of claim 29, wherein the antigen is a fungal antigen.

33. (New) The method of claim 29, wherein the antigen is a parasitic antigen.

34. (New) The method of claim 18, wherein the protein is an antibody.

35. (New) The method of claim 34, wherein the antibody is a monoclonal antibody.

36. (New) The method of claim 18, wherein the protein is a clotting factor.

37. (New) The method of claim 18, wherein the protein is a protease.

38. (New) The method of claim 18, wherein the protein is a pituitary hormone.

39. (New) The method of claim 18, wherein the protein is a protease inhibitor.

40. (New) The method of claim 18, wherein the protein is a growth factor.

41. (New) The method of claim 18, wherein the protein is a somatomedian.

42. (New) The method of claim 18, wherein the protein is an immunoglobulin.

43. (New) The method of claim 18, wherein the protein is a gonadotrophin.

44. (New) The method of claim 18, wherein the protein is a chemotactin.

45. (New) The method of claim 18, wherein the protein is a chemokine.

46. (New) The method of claim 18, wherein the protein is a plasma protein

47. (New) The method of claim 18, wherein the protein is a plasma protease inhibitor.

48. (New) The method of claim 18, wherein the protein is an interleukin.

49. (New) The method of claim 18, wherein the protein is an interferon.

50. (New) The method of claim 18, wherein the protein is a cytokine.

51. (New) A method of delivering a secreted protein into the bloodstream of a mammalian

subject, the method comprising:

introducing into the gastrointestinal tract of a mammalian subject by suppository administration a construct comprising:

b) a nucleic acid molecule comprising a coding sequence encoding a protein; and

c) a promoter sequence operably linked to the coding sequence operably linked to the coding sequence, wherein said construct is not packaged in a viral particle, said introducing resulting in introduction of the construct into an intestinal epithelial cell, production of the encoded protein in the intestinal epithelial cell and secretion of the protein from the cell and into the bloodstream of the subject. --